REMARKS

Upon entry of the foregoing amendment, claim 24 and claims 28-31 are pending in this application. Claims 1-23, and 25-27 have been withdrawn from examination as being directed to a non-elected invention. Claims 28-31 are newly added.

Claim 24 has been amended. Support for the amendment to claim 24 is found, *inter alia*, in original claim 24; on page 4, lines 6-7; and, page 19, lines 10-22. Claims 28-31 are newly added. Support for newly added claims 28-31 is found, *inter alia*, on page 16, lines 16-22, and elsewhere throughout the specification.

The specification has been amended at page 15, lines 5-22, to insert the sequence identifier number after the sequence. As amended, the specification now complies with the sequence rules.

It is believed no new matter has been added. In view of the amendments and following remarks, reconsideration of the rejections and withdrawal thereof is respectfully requested.

Restriction

At page 2 of the Office Action, Applicants acknowledge the Finality of the Restriction Requirement. Applicants reserve the right to file the non-elected claims in one or more divisional or continuation applications without prejudice.

Information Disclosure Statement

At page 2 of the Office Action, the Office has requested Applicants file or refile the PTO 1449 forms for proper consideration of the documents since only one PTO 1449 form was present at the time of examination. However, only one PTO 1449 was filed on February 16, 2001. There were additional Information Disclosure Statements filed on March 16, 2002, and on September 14, 2001, bringing the International Search Report (March 16, 2002) and a translation

of an International Preliminary Examination Report (IPER) (September 14, 2001) to the attention of the Examiner.

The Disclosure Statements filed in March and September of 2002 were not intended to include a PTO 1449 form, explaining why corresponding PTO 1449 forms were not present in the file. English language translations of the ISR and IPER were submitted for the Examiner's convenience in considering these documents. The publications referred to in these documents were submitted with the IDS filed February 16, 2001 which included a PTO 1449 form. While on occasion PCT forms listed on a PTO 1449 have been objected to by the U.S. PTO, Applicants will submit such forms listing the reports at the Examiner's request.

Applicants note that an additional Information Disclosure Statement was filed on May 23, 2003, listing documents cited on the Supplementary Partial European Search Report. The Examiner is respectfully requested to consider the documents cited thereon and return a signed, dated and initialed PTO 1449 form to the undersigned with the next communication.

Objection to the Specification

At page 3 of the Office Action, the specification is objected to for failing to reflect the priority status of the present application. In response thereto, Applicants have amended the specification accordingly.

At page 3 of the Office Action, the specification is objected to for improper disclosure of amino acid sequences without reference to a sequence identifier. However, the cited sequences "Arg Phe Lys Met" and "Arg Leu Lys Met" are the last four amino acids on the C terminus of their respective peptides and the 4-amino acid sequences are disclosed in the present sequence listing as SEQ ID NO: 9 and SEQ ID NO: 10, respectively. The specification has been amended to correctly position the sequence identifier number next to the four amino acid sequence it identifies. Since the sequences have previously been properly disclosed in both the paper copy of the sequence listing and the computer readable form (CRF) as is required by 37 CFR §§1.821-1.825, the application is in compliance with the sequence rules. In view of the amendments and arguments above, reconsideration and withdrawal of the objections is respectfully requested.

Objections to the claims

At page 4 of the Office Action, claim 24 is objected to for reciting using a substance that "inhibits the action due to CXCR4" to a mammal in need thereof. The marked-up version reflects claim 24 as previously amended in a preliminary amendment filed September 22, 2000. The amendments to the claim are believed to overcome the objection and withdrawal of the objection is respectfully requested.

Rejection under 35 USC § 102(b) over USPN 5,563,048 (Honjo *et al.*)

At page 4 of the Office Action, the Office rejected claim 24 under 35 USC § 102(b) as being anticipated by Honjo *et al.* (U.S. Patent No. 5,563,048; issued 1994)[Honjo]. Applicants respectfully traverse the rejection.

The Honjo document is cited to show SDF-1 polypeptides and their use in the treatment of diseases such as cancer. The Office argues that Honjo, while not specifically teaching the use of said substance to "suppress vascularization" or "inhibit the action due to CXCR4," teaches the use of pharmaceutical compositions comprising anti-SDF-1 antibodies or SDF-1 "structure resembling" polypeptides which inherently suppress vascularization and inhibit the action due to CXCR4.

However, Applicants disagree with the inherency argument. Although Honjo teaches the expression and isolation of the SDF-1 polypeptides, the pharmacological activity of the polypeptides has not been provided in the disclosure. Many indications for the peptides are, nevertheless, listed in the document, which even include abnormal proliferation of hematopoietic cells. While one named disease, cancer, may be related to "vascularization," Applicants respectfully disagree with the Examiner that undergrown or abnormal proliferation of hematopoietic cells is the same as vascularization.

More importantly, this exhaustive listing is not based on any tested or demonstrated activities, but is merely speculative. The so-named indications have been put forward because 1) the polypeptides are produced and secreted in pro-B cells (column 5, lines 17-31) and 2) mouse

SDF-1α was known to stimulate the proliferation of the mouse myeloid progenitor cell line DA1G in the laboratory test (column 5, lines 32-36).

The Honjo document is thus deficient in teaching the alleged utility of the polypeptides as possible therapeutics for suppressing vascularization by inhibiting the action of CXCR4. Specifically, or generally, Honjo does not teach "suppressing vascularization comprising administering a substance that inhibits the action of CXCR4 in a mammal in need thereof" using the SDF-1 polypeptides.

The Honjo document fails to teach, inherently or otherwise, each and every element of the claim. Accordingly, claim 24 (as amended), and new claims 28-31, are not anticipated by Honjo *et al.* In view of the arguments and amendments to the claims, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 102(b) over Arisawa *et al.*

At page 4 of the Office Action, the Office rejected claim 24 under 35 USC § 102(b) as being anticipated by Arisawa *et al.* (Arisawa *et al.*, *Annals of Surgical Oncology 2(2)*: 114-120 (1995) [Arisawa]). Applicants respectfully traverse the rejection.

The Office cited the Arisawa document to show dexamethasone displays antiangiogenic activity. The precise mechanism by which dexamethasone inhibits tumor angiogenesis is not described in the document and the failure to describe the mechanism is acknowledged by the Examiner. More importantly, however, is that newly amended claim 24 now recites that said substance is not dexamethasone. Accordingly, claim 24 (as amended), and new claims 28-31, are not anticipated by Arisawa *et al.* In view of the arguments and amendments to the claims, reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Reconsideration and the timely allowance of the pending claims is respectfully requested. A favorable action is awaited. Should the Examiner find that an

interview would be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a Constructive Petition for Extension of Time in accordance with 37 C.F.R § 1.136(a)(3).

Respectfully submitted,
Morgan, Lewis & Bockius LLP

Dated: **June 11, 2003**
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania, N.W.
Washington, D.C. 20004
202-739-3000

Suzanne E. Ziska
Registration No. 43,371

MARKED UP VERSION OF THE CHANGES TO THE SPECIFICATION

Claim 1 has been amended as follows:

24 (Twice Amended). A method for suppressing vascularization comprising administering a substance that inhibits the action of [due to] CXCR4 in [to] a mammal in need thereof, wherein said substance is not dexamethasone.

Claims 28-31 are newly added:

28. (New) The method of claim 24 wherein the substance is a substance based on inhibition of the binding itself between the ligand (SDF-1) and the receptor CXCR4.

29. (New) The method of claim 24 wherein the substance is a substance based on inhibition of the signaling from CXCR4 to nuclei.

30. (New) The method of claim 24 wherein the substance is a substance that inhibits the expression of CXCR4 itself.

31. (New) The method of claim 24 wherein the substance is a substance that inhibits the expression of SDF-1 itself.

The specification has been amended as follows:

A paragraph has been added on page 1, after line 2, as follows:

This application is a national stage filing of PCT/JP99/01448, filed March 23, 1999, which claims benefit to Japanese Patent Application No. 10/95448, filed March 24, 1998.

The paragraph at page 15, lines 5-14, has been replaced with the following paragraph:

Also, the amino acid sequence of SDF-1, which is a ligand binding to CXCR4, has already been known. There are two types of SDF-1 differing in the length of amino acid sequence, i.e., SDF-1-α and SDF-1-β. Specifically, the amino acid sequence of human SDF-1-α is set forth in SEQ ID NO: 5 and its base sequence in SEQ ID NO: 6 (base positions 474-740). Human SDF-1- β [(SEQ ID NO: 9)] is derived from human SDf-1- α by appending four amino acid residues, Arg Phe Lys Met (SEQ ID NO: 9), to a C-terminus thereof.

The paragraph at page 15, lines 15-22, has been replaced with the following paragraph:

The amino acid sequence of murine SDF-1- α is set forth in SEQ ID NO: 7 and its base sequence in SEQ ID NO: 8 (base positions 82-348). Murine SDF-1-β [(SEQ ID NO: 10)] is derived from murine SDF-1- α by appending four amino acid residues, Arg Leu Lys Met (SEQ ID NO: 10), to a C-terminus thereof. For human and murine SDF-1's, the sequence of from the 1st amino acid (Met) to the 21st amino acid (Gly) is a signal sequence.